

REMARKS

Pending claims

Claims 1-20 are currently pending as the claims for which Applicants have paid. Claims 21-56 were intended to be cancelled as stated in Item 13 of the "Transmittal Letter to the United States Designated/Elected Office (DO/EO/US) Concerning a Filing under 35 U.S.C. 371). By this Amendment, Applicants again request the cancellation claims 21-56. Applicants submit that these claims were included in the application as filed in interest of providing notice to the public of certain specific subject matter intended to be claimed, and were intended to be canceled at the time of filing this application in the interest of reducing filing costs. Applicants expressly state that these claims are **not** being canceled for reason related to patentability, and are in fact fully supported by the specification as filed. Applicants expressly reserve the right to reinstate these claims or to add other claims during prosecution of this application or a continuation or divisional application. Applicants expressly do not disclaim the subject matter of any invention disclosed herein which is not set forth in the instantly filed claims.

By this Amendment, claims 2, 3, 7, 8, 11, 14, and 18 are also cancelled. Amendment of claims 13 and 16 and addition of new claims 57-63 serve to further clarify the subject matter which applicants consider to be the invention. Support for new claims 57, may be found, for example, at page 23, line 15 of the specification. Support for new claims 58-63 may be found, for example, at page 8, lines 40-41, page 11, lines 8-10, and page 24, lines 3-14 of the specification. No new matter is added by any of these amendments.

Restriction Requirement

In the Restriction Requirement, the Examiner requested Applicants to elect one of the following inventions:

Group I (claims 1-10, 12, 16-17, 22-28, and 43-56) drawn to nucleic acids of SEQ ID NO:1-14. A microarray, methods of detecting nucleic acids of SEQ ID NO: 1-14, cells, method of producing a polypeptide.

Group II (claims 13, and 29-42) drawn to polypeptides. **Applicants noticed that the Restriction Requirement contained an apparent typographical error in that claim 12 was included instead of claim 13.**

Group III (claim 14) drawn to an antibody which binds to a disease detection and treatment molecule polypeptide.

Group IV (claim 11) drawn to a transgenic organism.

Group V (claim 15) drawn to a method of identifying a test compound which binds to a polypeptide.

Group VI (claims 18, 20) drawn to a method for screening a compound for effectiveness in altering expression of a target polynucleotide.

Group VII (claims 19, 21) drawn to a method of toxicity testing of a compound.

Applicants hereby elect, with traverse, to prosecute Group I, which corresponds to claims 1, 4, 5, 6, 9, 10, 12, 16, 17, and the newly added claims 57-63. Newly added claims 57-63 replace original claims 21-23, and 25-28, and are drawn to substantially the same invention.

Applicants also respectfully submit that there is minimal additional burden on the Examiner to examine claim 13, (Group II), claim 15 (Group V), claim 20 (Group VI), and claim 19 and newly added claim 57 (Group VII).

Further, in response to the requirement for election of a sequence, Applicants provisionally elect the polynucleotide species of SEQ ID NO:4, also with traverse. Applicants traverse both the restriction requirement and the obligation to elect a single sequence for prosecution which were imposed in the Office Action mailed December 18, 2002 for at least the following reasons.

The unity of invention standard *must* be applied in national stage applications

Section 1850 of the Manual of Patent Examining Procedure (original 8th edition, published August, 2001) (hereinafter "MPEP") provides:

... [W]hen the Office considers international applications ... during the national stage as a Designated or Elected Office under 35 U.S.C. 371, PCT Rule 13.1 and 13.2 will be followed

when considering unity of invention of claims of different categories without regard to the practice in national applications filed under 35 U.S.C. 111....

In applying PCT Rule 13.2 to ... national stage applications under 35 U.S.C. 371, examiners should consider for unity of invention all the claims to different categories of invention in the application and permit retention in the same application for searching and/or preliminary examination, claims to the categories which meet the requirements of PCT Rule 13.2....

Id at page 1800-60 to -61.

MPEP section 1893.03(d) reiterates the Examiner's obligation to apply the Unity of Invention standard PCT Rule 13.2 instead of U.S. restriction/election of species practice:

Examiners are reminded that unity of invention (not restriction) practice is applicable ... in national stage (filed under 35 U.S.C. 371) applications.

Id at page 1800-149, column 1.

Specific provisions of the Administrative Regulations Under the PCT and the corresponding provisions of the MPEP strongly support a finding of unity of invention among all of the claims in the present case

Unity of Invention is accepted as between claim 13 directed to polypeptide sequences and claim 1 directed to the polynucleotide sequences which encode them

Example 17, Part 2 of Annex B to the Administrative Instructions Under the PCT provides that unity of invention is accepted as between claims to polypeptide sequences and claims to polynucleotide sequences encoding those polypeptides. Those Examples are cited in MPEP section 1893.03(d) at page 1800-149, column 2 (“[n]ote also examples 1-17 of Annex B Part 2 of the PCT Administrative Instructions...”)

Thus, in the present case, unity of invention exists as between claims drawn to polypeptide sequences (*i.e.*, claim 13) and as to claims drawn to polynucleotide sequences (*i.e.*, claims 1, 4, 9, 10, 16, 58-63), as least with respect to each individual polypeptides and the polynucleotide sequences which encode it.

Therefore, Applicants respectfully request that the Examiner withdraw the Restriction Requirement at least as to claims 1, 4, 9, 10, 13, 16, and 58-63 and examine those claims in a single application.

Unity of invention exists with respect to dependent claims in the same claim category as the independent claim from which they depend

MPEP section 1850(A) and 1893.03(d), which recite the provisions of paragraph (c) of Part 1 (entitled “Instructions Concerning Unity of Invention”) of Annex B (entitled “Unity of Invention”) to the Administrative Instructions Under the PCT, provides:

(A) Independent and Dependent Claims.

Unity of invention has to be considered in the first place only in relation to the independent claims in an international application and not the dependent claims. By “dependent” claim is meant a claim which contains all the features of another claim and is in the same category of claim as that other claim (the expression “category of claim” referring to the classification of claims according to the subject matter of the invention claimed for example, product, process, use or apparatus or means, etc.).

(i) If the independent claims avoid the prior art and satisfy the requirement of unity of invention, no problem of lack of unity arises in respect of any claims that depend on the independent claims. In particular, it does not matter if a dependent claim itself contains a further invention....

See MPEP section 1850(A) at page 1800-61. See also MPEP Appendix AI at page 53.

In the present case, claims 4, 9-10, 12-13, and 58-63, all of which depend from claim 1, are all directed to compositions of matter, *i.e.*, to products. All of these claims contain all of the features of the independent claim. Further, as discussed above, there is unity of invention as between claim 1 and claim 13.

Thus, it is improper to restrict claims 1, 2, 16 and 17 from claims 3-8 and 11, as the Examiner has done. Therefore, Applicants respectfully request that the Examiner withdraw the Restriction Requirement at least as to the composition of matter claims, and that at least those claims be considered together in a single application.

In the event that the Examiner does not apply the unity of invention standard to this national phase application, Applicants note that the invention encompassed by claims 19, 20, and 57 are drawn to methods of use of the polynucleotides of Group I, and should be examined together. These method claims recite a product (*i.e.*, a polynucleotide), which is of the same scope as the claimed polynucleotides being searched by the Examiner. Therefore, it would not be an undue burden on the

Examiner to examine these method claims since the searches for the claimed polynucleotides and these method claims would substantially overlap.

In addition, the method claims 19, 20, and 57 are entitled to rejoinder upon allowance of a product claim per the Commissioner's Notice in the Official Gazette of March 26, 1996, entitled "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b)" which sets forth the rules, upon allowance of a product claim, for rejoinder of process claims covering the same scope of products. See also M.P.E.P. 821.04 as follows.

Where product and process claims drawn to independent and distinct inventions are presented in the same application, applicant may be called upon under 35 U.S.C. 121 to elect claims to either the product or process. . . The claims to the nonelected invention will be withdrawn from further consideration under 37 C.F.R. 1.142. . . . However, if applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims which depend from or otherwise include all the limitations of the allowable product claim will be rejoined.

The Election of Species Requirement

Applicants elect, with traverse, to prosecute claims related to the polynucleotide sequences of SEQ ID NO:4. Those polynucleotide sequences read on claims 1 and 4.

Applicants traverse the Election of Species Requirement for at least the following reasons.

The Examiner's attention is directed to the Patent Office's own requirements for Markush practice, set forth in the 7th edition of the M.P.E.P. (July 1998) at § 803.02 regarding restriction requirements in Markush-type claims:

PRACTICE RE MARKUSH-TYPE CLAIMS

If the members of the Markush group are **sufficiently few in number or so closely related** that a search and examination of the entire claim can be made without serious burden, the examiner must examine all claims on the merits, even though they are directed to independent and distinct inventions. In such a case, the examiner will not follow the procedure described below and will not require restriction.

Since the decisions in *In re Weber*, 580 F.2d 455, 198 USPQ 328 (CCPA 1978) and *In re Haas*, 580 F.2d 461, 198 USPQ 334 (CCPA 1978), **it is improper for the Office to refuse to examine that which applicants regard as their invention**, unless the subject

matter in a claim lacks unity of invention. *In re Harnish*, 631 F.2d 716, 206 USPQ 300 (CCPA1980); and *Ex parte Hozumi*, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984).

Broadly, **unity of invention exists where compounds included within a Markush group (1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility.**

This subsection deals with Markush-type generic claims which include a plurality of alternatively usable substances or members. In most cases, a recitation by enumeration is used because there is no appropriate or true generic language. A Markush-type claim can include independent and distinct inventions. This is true where two or more of the members are so unrelated and diverse that a prior art reference anticipating the claim with respect to one of the members would not render the claim obvious under 35 U.S.C. 103 with respect to the other member(s). In applications containing claims of that nature, **the examiner may require a provisional election of a single species** prior to examination on the merits. The provisional election will be given effect in the event that the Markush-type claim should be found not allowable. Following election, the Markush-type claim will be examined fully with respect to the elected species and further to the extent necessary to determine patentability. If the Markush-type claim is not allowable over the prior art, examination will be limited to the Markush-type claim and claims to the elected species, with claims drawn to species patentably distinct from the elected species held withdrawn from further consideration.

As an example, in the case of an application with a Markush-type claim drawn to the compound C-R, wherein R is a radical selected from the group consisting of A, B, C, D, and E, the examiner may require a provisional election of a single species, CA, CB, CC, CD, or CE. The Markush-type claim would then be examined fully with respect to the elected species and any species considered to be clearly unpatentable over the elected species. If on examination the elected species is found to be anticipated or rendered obvious by prior art, the Markush-type claim and claims to the elected species shall be rejected, and claims to the nonelected species would be held withdrawn from further consideration. As in the prevailing practice, a second action on the rejected claims would be made final.

On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a nonelected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. The prior art search, however, will not be extended unnecessarily to cover all nonelected species. Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated or rendered obvious by the prior art, the amended Markush-type claim will be reexamined. The prior art search will be extended to the extent necessary to determine patentability of the Markush-type claim. In the event prior art is found during the reexamination that anticipates or renders obvious the amended Markush-type claim,

the claim will be rejected and the action made final. Amendments submitted after the final rejection further restricting the scope of the claim may be denied entry. [emphasis added]

As can be seen from the above, it is clear that the present Restriction Requirement does not meet the Patent Office's own requirements.

First, if the number of "members of the Markush group are **sufficiently few in number or so closely related** that a search and examination of the entire claim can be made without serious burden, the examiner must examine all claims on the merits, even though they are directed to independent and distinct inventions. **In such a case, the examiner will not follow the procedure described below and will not require restriction.**" Withdrawal of the restriction requirement as between the specific sequences each in the claims is required on that basis alone.

Second, **"it is improper for the Office to refuse to examine that which applicants regard as their invention**, unless the subject matter in a claim lacks unity of invention. ... Broadly, **unity of invention exists where compounds included within a Markush group (1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility.**" Clearly, the sequences of the instant invention share both a common utility and structural homology, based on their classification as human transport proteins, and their possession of common structural features, such as transmembrane domains.

Third, even if the claims could be considered to be "Markush-type generic claims which include a plurality of alternatively usable substances or members," it is further noted that the M.P.E.P states that "A Markush-type claim can include independent and distinct inventions. This is true where two or more of the members are so unrelated and diverse that a prior art reference anticipating the claim with respect to one of the members would not render the claim obvious under 35 U.S.C. 103 with respect to the other member(s). In applications containing claims of that nature, **the examiner may require a provisional election of a single species** prior to examination on the merits." This clearly applies in the present case.

Finally, the Examiner's attention is directed to the M.P.E.P. at § 803.04 (Restriction - Nucleotide Sequences, EXAMPLES OF NUCLEOTIDE SEQUENCE CLAIMS) which states:

Applications claiming more than ten individual independent and distinct nucleotide sequences in alternative form, such as set forth in example (A), will be subject to a restriction requirement. Only the ten nucleotide sequences selected in response to the restriction requirement and any other claimed sequences which are patentably indistinct therefrom will be examined.

Applications claiming only a combination of nucleotide sequences, such as set forth in example (B), will generally not be subject to a restriction requirement. The presence of one novel and nonobvious sequence within the combination will render the entire combination allowable. The combination will be searched until one nucleotide sequence is found to be allowable. The order of searching will be chosen by the examiner to maximize the identification of an allowable sequence. If no individual nucleotide sequence is found to be allowable, the examiner will consider whether the combination of sequences taken as a whole renders the claim allowable.

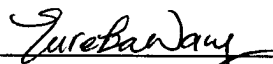
Therefore, it is respectfully submitted that, upon searching and examining SEQ ID NO:4 and finding no prior art over which SEQ ID NO:4 can be rejected, the Examiner must extend the search of the Markush-type claim to include 13 additional non-elected species.

CONCLUSION

Please charge Deposit Account No. **09-0108** in the amount of **\$110** as set forth in the enclosed fee transmittal letter. If the USPTO determines that an additional fee is necessary, please charge any required fee to Deposit Account No. **09-0108**.


Respectfully submitted,
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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claims 2, 3, 7, 8, 11, 14, and 18 are canceled.

Claims 13 and 16 have been amended.

Claims 57-63 have been added.

13 (Once Amended). A purified disease detection and treatment molecule polypeptide (MDDT) encoded by at least one of the polynucleotides of claim [2]1.

16 (Once Amended). A microarray wherein at least one element of the microarray is a polynucleotide of claim [3]1.

57 (New). A method for assessing toxicity of a test compound, said method comprising:

- a) treating a biological sample containing nucleic acids with the test compound;
- b) hybridizing the nucleic acids of the treated biological sample with a probe comprising at least 20 contiguous nucleotides of a polynucleotide of claim 1 under conditions whereby a specific hybridization complex is formed between said probe and a target polynucleotide in the biological sample, said target polynucleotide comprising a polynucleotide sequence of a polynucleotide of claim 1 or fragment thereof;
- c) quantifying the amount of hybridization complex; and
- d) comparing the amount of hybridization complex in the treated biological sample with the amount of hybridization complex in an untreated biological sample, wherein a difference in the amount of hybridization complex in the treated biological sample is indicative of toxicity of the test compound.

58 (New). An array comprising different nucleotide molecules affixed in distinct physical locations on a solid substrate, wherein at least one of said nucleotide molecules comprises a first

oligonucleotide or polynucleotide sequence specifically hybridizable with at least 30 contiguous nucleotides of a target polynucleotide, said target polynucleotide having a sequence of claim 1.

59 (New). An array of claim 58, wherein said first oligonucleotide or polynucleotide sequence is completely complementary to at least 30 contiguous nucleotides of said target polynucleotide.

60 (New). An array of claim 58, which is a microarray.

61 (New). An array of claim 58, further comprising said target polynucleotide hybridized to said first oligonucleotide or polynucleotide.

62 (New). An array of claim 58, wherein a linker joins at least one of said nucleotide molecules to said solid substrate.

63 (New). An array of claim 58, wherein each distinct physical location on the substrate contains multiple nucleotide molecules having the same sequence, and each distinct physical location on the substrate contains nucleotide molecules having a sequence which differs from the sequence of nucleotide molecules at another physical location on the substrate.